procedure. The GTP did not compete with the m7guanosine-BSA whereas the m7 versions all competed efficiently.

Having now fully described the present invention in some detail by way of illustration and example for purposes of clarity of understanding, it will be obvious to one of ordinary skill in the art that the same can be performed by modifying or changing the invention within a wide and equivalent range of conditions, formulations and other parameters without affecting the scope of the invention or any specific embodiment thereof, and that such modifications or changes are intended to be encompassed within the scope of the appended claims.--

In the Claims:

Marked copies of the claim revisions, but not the new claims, have been provided in the attached Appendix I.

Please amend claims 1-7 to read as follows:

--1 (amended). A method to produce one or more cDNA molecules comprising:

(a) contacting a sample comprising an mRNA template with a solid medium, wherein the solid medium comprises a matrix;

(b) sorbing at least a portion of the mRNA template to the solid medium; and

(c) contacting the template with one or more reverse transcriptases under conditions sufficient to synthesize one or more cDNA molecules complementary to all or a portion of the templates.

2 (amended). The method of claim 1, wherein the cDNA is a cDNA library.

3 (amended). The method of claim 1, wherein the mRNA template is removed from the solid medium prior to the cDNA synthesis.

4 (amended). The method of claim 1, wherein the cDNA is double-stranded.

5 (amended). The method of claim 1, further comprising:

(d) amplifying the cDNA.

6 (amended). A method for storing an mRNA molecule, comprising:

(a) contacting a cell comprising an mRNA molecule to be stored with a solid medium, wherein the solid medium comprises a matrix containing a composition for substantially inhibiting degradation of the mRNA molecule; and

(b) drying the cell and the solid medium.

7 (amended). The method of claim 6, wherein the composition comprises:

(a) a weak base;

(b) a chelating agent; and

(c) an anionic detergent or surfactant.--

Please add the following new claims:

--8 (new). The method of claim 1, wherein the matrix contains a composition for substantially inhibiting degradation of the mRNA template, the composition comprising:

(a) a weak base;

(b) a chelating agent; and

(c) an anionic detergent or surfactant.

9 (new). The method of claim 8, wherein the composition further comprises uric acid or a urate salt.

10 (new). The method of claim 1, wherein the matrix comprises a cellulose-based matrix or paper, or a micromesh of synthetic plastic material.

11 (new). The method of claim 1, wherein the solid medium is selected from the group consisting of nitrocellulose, cellulose, diazocellulose, carboxymethylcellulose, hydrophilic polymers, polytetra-fluoro-ethylene, fiberglass, porous ceramics, polystyrene, polyvinylchloride, polypropylene, polyethylene, dextran, agarose, agar, starch, and nylon.

12 (new). The method of claim 1, wherein the sample comprising the mRNA template is selected from the group consisting of cells, viruses, viral plaques, and preparations from biological materials.

13 (new). The method of claim 7, wherein the composition further comprises uric acid or a urate salt.

14 (new). The method of claim 6, wherein the matrix comprises a cellulose-based matrix or paper, or a micromesh of synthetic plastic material.

15 (new). The method of claim 6, wherein the solid medium is selected from the group consisting of nitrocellulose, cellulose, diazocellulose, carboxymethylcellulose, hydrophilic polymers, polytetra-fluoro-ethylene, fiberglass, porous ceramics, polystyrene, polyvinylchloride, polypropylene, polyethylene, dextran, agarose, agar, starch, and nylon.

16 (new). The method of claim 1, wherein the sample comprising the mRNA template is selected from the group consisting of cells, viruses, viral plaques, and preparations from biological materials.--

## REMARKS

### I. Status of the Claims

Claims 1-16 are pending in the application with claims 1 and 6 being the independent claims. Claims 1-7 have been amended, and new claims 8-16 have been added.

The amendments to claims 2 and 4-5 are primarily stylistic. Support for the amendments to claims 1, 3, and 6-7 and for new claims 8-16 can be found throughout the specification as originally filed, particularly on pages 7-12. Additional support for the amendments to claims 1, 3, and 6 can be found on page 7, lines 21-25. Additional support for the amendments to claims 7 and for new claims 8-10 and 13-14 can be found on page 7, lines 25-30, and on page 8, lines 1-2. Additional support for new claims 11 and 15 can be found on page 8, lines 3-8. Additional support for new claims 12 and 16 can be found on page 8, lines 18-21.

**II. The Drawings Have Been Corrected**

The Draftsperson objected to the drawings (Figures 1-4) due to unacceptable left margins. The drawings have been corrected accordingly.

**III. The Priority Claim Has Been Corrected**

The Examiner has required correction of the priority claim with respect to the priority claim and to the format of the priority claim in a single sentence. Applicant has amended the specification accordingly. Applicant claims priority to United States Provisional Application 60/175,307, filed January 10, 2000.

**IV. The Examiner's Request for a New Oath or Declaration Has Been Accommodated**

The Examiner maintained that the declaration previously filed was defective for reasons relating to the priority claim. Applicants hereby furnish new declarations in response to the Examiner's request.

**V. The Examiner's Comments Concerning the Information Disclosure Statement Have Been Addressed**

The Examiner has noted that references not cited by the Examiner on form PTO-892 have not been considered. Applicants hereby submit an additional IDS herewith.

**VI. The Examiner's Comments Concerning the Title Have Been Addressed**

The Examiner has maintained that the "title of the invention is not descriptive." Applicants hereby request the Examiner to amend the title as noted above.

**VII. The Examiner's Request for the Incorporation of Material into the Specification Has Been Accommodated by Amendment of the Specification**

The Examiner has maintained:

> The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application.

The Examiner also noted:

> The attempt to incorporate subject matter into this application by reference to a provisional and to a non-provisional US patent is improper because these applications are being relied upon for enablement of applicant's preferred embodiment. See page 19, lines 15-18.

Pursuant to the Examiner's request, Applicants have amended the specification (above) to include the pertinent portions of U.S. Patent Application 09/076,115 and U.S. Provisional Patent Application 60/122,395, filed March 2, 1999, according to purported copies of these applications obtained from the patent practitioner of their owner, because

neither of these applications belongs to the Assignee or the Applicants in this case. Asterisks (* * *) indicate material not included from the original applications.

A declaration by a practitioner representing Applicants is also hereby submitted.

Based on the previous reference to the U.S. patent application and U.S. provisional patent application, Applicants maintain that no new matter has been added by virtue of the amendment made to the specification.

**VIII. Applicants Have Provided a Sequence Listing in Compliance with 37 CFR 1.821(a)(1) and (a)(2)**

Applicants request the Examiner to enter the changes in the specification requested above with regard to the Sequence Listing.

Applicants submit herewith Sequence Listing pages 1-4 to include as a sequence listing as part of this Application (renumbered as pages inserted at the end of the specification and before the claims). The substitute pages are provided in paginated and unpaginated format.

No new matter has been added by virtue of the amendment made to the specification.

Further enclosed is a computer readable copy of the above-mentioned copy of the Sequence Listing. That copy is the same as the copy of the Sequence Listing.

Also enclosed is a Statement in Support of Filing and Submissions in Accordance with 37 CFR 1.821-1.825, which declares that the content of the paper and the computer readable copies of the Sequence Listing submitted in accordance with 37 CFR 1.821 (c) and (e), respectively, are the same and that the submission, filed in accordance with 37 CFR 1.821 (g) does not introduce new matter.

**IX. Rejection of Claims 1-7 Under 35 U.S.C. § 112, First Paragraph, Has Been Accommodated By Amendment of the Specification and Claims**

The Examiner rejected claims 1-7 under 35 U.S.C. 112, first paragraph, as "containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention."

The Examiner stated:

> As presently worded, the claims are drawn to a method whereby cDNA is produced. Upon review of the disclosure it is noted that the specification seeks to incorporate by reference disclosures in non-published US Patent Applications wherein these disclosures are of a preferred embodiment. As indicated above, applicant cannot incorporate by reference essential materials, which, as here, is deemed by applicant to be representative of their preferred embodiment. While applicant can incorporate by reference essential subject matter when it is found in a published US Patent, such latitude is not accorded when the document is a non-published application, be it from the US or otherwise.

As noted supra, Applicants have amended the specification to include the pertinent portions of the U.S. patent application 09/076,115 and the U.S. provisional patent application 60/122,395, as requested by the Examiner.

The Examiner further rejected claims 6-7 as "not enabled by the disclosure whereby any and all RNA in a cell is retained in a useful length when the cell is simply allowed to die and is dried, as is encompassed by the claims."

The Examiner stated:

> It is well known that RNA is highly sensitive to degradation yet the claimed method places no limitation on the manner in which the cell, and its RNA, be it tRNA, mRNA, rRNA or mitochondrial RNA is preserved *ad inifinitum*, without any precautions.

As noted *supra*, the specification has been amended to include the U.S. patent application 09/076,115 and U.S. provisional patent application 60/122,395, which were previously incorporated by reference on page 19. In addition, Applicants have amended claim 6 from "RNA" to "mRNA." The *verbatim* incorporation of pertinent sections of the specifications of the 09/076,115 and 60/122, 395 provides further enablement, in addition to the enablement found throughout the specification as filed (and particularly the Examples and pages 7-12), for claim 6, and by dependence, claim 7.

In view of the foregoing remarks, Applicants respectfully assert that the present invention is enabled. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejections made under 35 U.S.C. § 112, first paragraph.

**X. Rejection of Claims 6-7 Under 35 U.S.C. § 112, Second Paragraph, Is Accommodated by Amendment**

The Examiner has rejected claims 6-7 under 35 U.S.C. § 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." The Examiner has rejected the use of the trademark/trade name FTA in claim 7.

Applicants have hereby accommodated the Examiner's rejection by amendment of claim 7 to eliminate the use of the trademark/trade name FTA.

The Examiner also states that "[c]laim 6, from which claim 7 depends, is similarly rejected as an independent claim encompasses all of the limitations of the claims that depend therefrom." It is difficult to understand how an independent claim that would otherwise be

definite would suddenly become indefinite simply by the addition of an indefinite dependent claim. Applicants respectfully traverse rejection of claim 6. In addition, the Examiner's rejection of claim 6 due to the use of the trademark/trade name FTA in claim 7 is rendered moot by amendment of claim 7 to remove the reference to FTA.

In view of the foregoing remarks, Applicants respectfully assert that the present invention is not indefinite. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejections made under 35 U.S.C. § 112, second paragraph.

## XI. Rejection of Claims 1, 2, and 4 Under 35 U.S.C. § 102(e) (pre-AIPA) Is Traversed

The Examiner has rejected claims 1, 2, and 4 under 35 U.S.C. 102(e) (pre-AIPA) as being anticipated by Hornes et al. (U.S. Patent No. 5,759,820; granted 6/2/98; filed 7/25/94). This rejection is respectfully traversed.

The Examiner alleges that "Hornes et al., columns 6-8, disclose binding of mRNA to a solid support and then subjecting the isolated/immobilized mRNA to a reverse transcriptase so to produce a corresponding cDNA. The aspect of synthesizing a double-stranded cDNA is also disclosed therein."

Applicant respectfully submits that Hornes et al. do not anticipate claims 1, 2, and 4 of the present invention.

Hornes et al. describe a "Process for Producing cDNA," which includes contacting a liquid containing mRNA with an insoluble support having DNA probes attached via their respective 5'-termini whereby the mRNA is hybridized to the probes and hence to the support, followed by removal of the liquid and addition of enzymes and nucleotides such that the probe is used to produce single-stranded cDNA. The insoluble support includes magnetic particles (e.g., beads), which are monodisperse polymer particles (e.g., superparamagnetic

iron oxide); a coating (e.g., oligo-dA) to reduce non-specific binding; and a substituent (e.g., a nucleic acid-binding function group at the surface of the particle via chemical, affinity or other binding) for attaching an oligonucleotide (see abstract and claims). Essentially, Hornes et al. describe a process for producing cDNA using a system of magnetic beads with primers (preferably oligo-dT) attached.

Applicants respectfully assert that the mRNA of the claimed invention is not hybridized to probes, which are themselves attached to the solid medium or support. Rather, the mRNA is sorbed to the solid medium (e.g., as in claims 1, 2, and 4). The present invention does not require an insoluble support that includes magnetic particles, a coating comprising oligo-dA to reduce non-specific binding, or an attached oligonucleotide (e.g., oligo-dT).

In view of the foregoing remarks, Applicant respectfully asserts that the present invention is not anticipated by Hornes et al. Therefore, Applicant respectfully requests reconsideration and withdrawal of the rejections made under 35 U.S.C. § 102(e).

**XII. Rejection of Claim 6 Under 35 U.S.C. § 102(b) Is Traversed**

The Examiner has rejected claim 6 under 35 U.S.C. 102(b) as being anticipated by "a desert highway road kill". This rejection is respectfully traversed.

The Examiner also alleges:

As presently worded, all that is required for preservation of RNA in a cell is that the cell be contacted with a solid support and allowed to dry. Such limitations are readily achieved by the untimely demise of fauna on desert highways where they undoubtedly come into contact with a sold support and are allowed to dry, as is the case where insects are thinly and rapidly applied to a solid surface and are quickly brought to a desiccated state by the passing of a high rate of air flow over their remains.

Applicant respectfully submits that a desert highway road kill does not anticipate claim 6 of the present invention under § 102(b).

35 U.S.C. § 102(b) reads as follows:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States;

Applicants traverse this rejection as being without merit. Anticipation under §102(b) requires that "the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States" and the fact that none of these conditions applies. Even "public use" does not apply, because as the Examiner himself notes above, "[i]t is well known that RNA is highly sensitive to degradation yet the claimed method places no limitation on the manner in which the cell, and its RNA, be it tRNA, mRNA, rRNA or mitochondrial RNA is preserved *ad infinitum*, without any precautions" and certainly the above "desert highway roadkill" method is not a method intentionally used for that purpose by anyone, including one of ordinary skill in the pertinent art.

Applicants also traverse this rejection based on the current amendments to claim 6, which comprises a composition for substantially inhibiting the degradation of the mRNA molecule.

In view of the foregoing remarks, Applicant respectfully asserts that the present invention is not anticipated by a desert highway road kill. Therefore, Applicant respectfully requests reconsideration and withdrawal of the rejections made under 35 U.S.C. § 102(b).

**XIII. Rejection of Claims 1-5 Under 35 U.S.C. § 102(b) Is Traversed**

The Examiner has rejected claims 1-5 under 35 U.S.C. 102(b) as being anticipated by Pharmacia Biotech Catalog (1994). This rejection is respectfully traversed.

The Examiner alleges:

> Pharmacia Biotech Catalog (1994), page 119, discloses for sale spin columns that are packed with oligo(dT)-cellulose and that these solid supports are used in the isolation of mRNA, and its subsequence use in the synthesis of cDNA and in polymerase chain reaction; a type of nucleic acid amplification assay.

The Examiner also alleges:

> While the catalog does not speak explicitly of the cDNA being double-stranded, such is considered an inherent property in view of the cDNA being used on a PCR assay which is predicated upon the use of primer pairs where one primer is directed to each strand of a double-stranded template (cDNA).

Applicants respectfully submit that Pharmacia Biotech Catalog does not anticipate claims 1-5 of the present invention.

Applicants submit that cDNA is not inherently double-stranded. In the present invention, cDNA may be single-stranded. Most reverse transcriptases have RNase activity, thereby destroying the RNA template from which the cDNA is derived. PCR can occur with a single-stranded template. The first cycle will only allow binding of one primer. In such a case, during the first cycle, a second strand is synthesized, allowing "traditional" two-primer amplification to occur in the subsequent cycles. Thus, molecules of interest in this application are usually single-stranded prior to the amplification event.

Essentially, the Pharmacia spin columns appear to consist of cellulose with attached oligo-dT primers for hybridization to the poly-A tails of mRNA molecules. As noted *supra* with respect to Hornes et al., Applicants respectfully assert that the mRNA of the claimed

invention is not hybridized to probes, which are themselves attached to the solid medium or support. Rather, the mRNA is sorbed to the solid medium (e.g., as in claims 1-5). The present invention does not require an insoluble support that includes an attached oligonucleotide (e.g., oligo-dT).

In view of the foregoing remarks, Applicant respectfully asserts that the present invention is not anticipated by Pharmacia Biotech Catalog. Therefore, Applicant respectfully requests reconsideration and withdrawal of the rejections made under 35 U.S.C. § 102(b).

## IX. Conclusion

In view of the foregoing amendments and remarks, the present application is respectfully considered in condition for allowance. An early reconsideration and notice of allowance are earnestly solicited.

It is believed that all outstanding rejections have been addressed by this submission and that all the claims are in condition for allowance. If discussion of any amendment or remark made herein would advance this important case to allowance, the Examiner is invited to call the undersigned as soon as convenient.

Applicants hereby request a three-month extension of time for the Amendment and accompanying materials. Although it is not believed that any additional fee (in addition to the fee concurrently submitted) is required to consider this submission, the Commissioner is hereby authorized to charge our deposit account no. 04-1105 should any fee be deemed necessary.

Respectfully submitted,

Date: Sept. 26, 2002

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